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EXAMINER	
MORAN, M	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	08/942,369	CHEN ET AL.	
	Examiner	Art Unit	
	Morjorie Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-24 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *30* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *detailed action* .

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Amended claims 20-24 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over JOHNSON (US 4,077,845) in view of LIBMAN *et al.* (US 4,046,138) and the MANUAL OF CLINICAL MICROBIOLOGY (MCB), and further in view of CARR *et al.* (IDS ref: US 5,064,756).

Applicant's arguments with respect to claims 20-24 have been considered but are moot in view of the new ground(s) of rejection. Arguments set forth in the response and CHEN declaration of 3/26/01 with regard to the combination of JOHNSON, LIBMAN, and the MCB are addressed below.

Claim 20 recites a method to simultaneously detect and determine the susceptibility of urinary pathogens to antimicrobial agents comprising (a) providing a multicompartment assay device with at least one compartment comprising a growth medium (capable of sustaining growth of total microbial organisms), at least one compartment comprising a uropathogenic specific medium (UTI medium) and at least one compartment comprising an antimicrobial susceptibility interpretation medium comprising an antimicrobial agent (interpretation medium), (b) placing a portion of the sample in each type of compartment, whereby metabolism of a signal generating substrate and production of a signal in the growth medium compartment indicates the presence of total microbial organisms, metabolism of a substrate and production of a signal in the UTI medium indicates the presence of uropathogens, and metabolism of a substrate and detection of a signal in the interpretation medium indicates that the organisms lack susceptibility to the antimicrobial agent in the interpretation medium, and (c) examining the

compartments to determine the presence of uropathogens in the samples and susceptibility thereof to antimicrobial agents. Claim 21 limits the sample to urine. Claim 22 limits the organisms detected to primary gram negative urinary pathogens. Claim 23 limits the pathogens of claim 22 to Enterobacteriacae. Claim 24 limits the pathogens of claim 22 to be selected from E. coli, Klebsiella spp., Enterobacter spp., Proteus mirabilis, Proteus vulgaris, Morganella morganii, Providencia retteri, and Acinobacter spp. It is again noted that the specification, on page 10, defines primary gram negative urinary pathogens as those which cause 85-90% of all urinary tract infections, which pathogens include but are not limited to E. coli, Klebsiella spp., Enterobacter spp., and Proteus mirabilis. It is further noted that the specification, on page 12, defines a uropathogenic specific medium as one which allows only the growth of primary gram negative urinary pathogens and allows for substantially less growth of any other bacteria.

JOHNSON, LIBMAN, and the MCB make obvious a method of simultaneously detecting and determining the antimicrobial susceptibility of urinary pathogens, as previously set forth. The MacConkey agar of LIBMAN comprises lactose and produces a pink/red color (signal) when the lactose is metabolized by galactosidase. JOHNSON, LIBMAN, and the MCB do not specifically teach a signal generating substrate (i.e. metabolism of lactose results in a signal but lactose itself does not generate the signal).

CARR teaches a method to determine the susceptibility of microorganisms to an antimicrobial substance wherein fluorogenic or chromogenic substrates (indicators) are added to a growth medium (abstract and col. 2, lines 45-68). CARR teaches that his substrates can be used to detect growth of various bacteria, including those recited in claim 24 (col. 7, lines 28-50). CARR further teaches that his method is an improvement as results can be obtained in as little as 4 hours (col. 2, lines 35-40).

It would have been obvious to one of ordinary skill in the art at the time of invention to have included the substrates of CARR in the medium in the method of JOHNSON, LIBMAN, and the MCB where the motivation would have been to improve the method of detection and determination of antibiotic susceptibility, as taught by CARR. One skilled in the art would reasonably have expected success in detecting and determining antibiotic susceptibility of the urinary pathogens in the method of JOHNSON, LIBMAN, and the MCB using the substrates of CARR because CARR teaches that growth microorganisms including those recited in the instant claims can be detected and antibiotic susceptibility determined using his substrates in growth media.

Applicant's argument that prior art methods require four steps whereas the inventive method requires only one is not relevant as JOHNSON does not teach that his method requires four steps. In fact, JOHNSON teaches only a single incubation step in his method (col's 10-12).

Applicant further argues in the response filed 3/26/01 that neither JOHNSON nor LIBMAN teach growth media. In response, it is noted that his growth wells comprise culture medium in which microorganisms can "live and propagate" and that when optical change is observed, "it is apparent that the specific microorganism is living in the culture medium" (col. 6, lines 48-60). JOHNSON further teaches that it is desirable to have at least one of the growth wells contain culture medium by itself whereas culture medium in other wells can have antibiotic blended with it (col. 7, lines 10-15), and teaches that "(g)rowth in individual growth wells permits a positive test for indication of organisms", (col. 7, lines 42-43). The examiner therefore maintains that JOHNSON teaches a growth medium. In response to the argument that LIBMAN does not teach a growth medium, it is noted that LIBMAN teaches use of "two or more different media, selective and nonselective" (col. 3, lines 64-66). As a "nonselective" medium is

presumably one which allows growth of all (or many) microorganisms in a sample, the examiner interprets LIBMAN's nonselecetive medium to be a growth medium.

In response to the argument that MacConkey agar of LIBMAN is not a uropathogenic specific medium, applicant's attention is again drawn to the teaching of LIBMAN that MacConkey agar is a "differential" (i.e. selective) medium which can readily identify "common gram negative organisms (*responsible for more than 90% of urinary tract infections*)", emphasis added by examiner. As set forth above, the specification teaches on page 12 that a uropathogenic specific medium is one which allows for growth of primary gram negative urinary pathogens and allows for substantially less growth of other organisms. The specification further defines "primary gram negative urinary pathogens" on page 10 as those which cause 85-90% of all urinary tract infections. Applicants argue in both the response filed 3/26/01 and the CHEN declaration that MacConkey agar is not a UTI medium as defined by the specification. The CHEN declaration refers to the Difco manual, which states that "MacConkey media are selective and differential plating media mainly used for the detection and isolation of gram-negative organisms..." This is not a teaching that MacConkey agar is not specific for uropathogens, but in fact, supports the teachings of LIBMAN that MacConkey agar is selective for gram-negative organisms. As the Difco manual further teaches that MacConkey agar can be used to differentiate between different types of gram negative bacteria, the Difco manual further provides support that MacConkey agar is not merely selective for ANY gram-negative bacteria, but is selective for particular types of gram-negative bacteria. As the gram-negative bacteria for which MacConkey agar is selective are described by LIBMAN as those which cause over 90% of urinary tract infections (i.e. a definition in concordance with that set forth in the specification for a "primary gram negative urinary pathogen"), the examiner maintains that the MacConkey agar of LIBMAN is a urinary pathogenic specific medium in concordance with the definition set

forth in the instant specification. The argument that CLED agar supports growth of contaminants is not germane as the rejection is not drawn to CLED agar. Arguments that MacConkey agar supports growth of contaminants is not supported by any evidence and is not germane, as the definition of a UTI medium set forth in the instant specification merely requires that the medium not allow "substantial" growth of any other organism. A selective agar is necessarily one which allows for growth of certain microorganisms while NOT allowing for growth of others. As MacConkey agar is taught to be selective for particular gram negative organisms, it is clear that "substantial" growth of other organisms is not "allowed". In response to the argument that MacConkey agar does not allow growth of Proteus, it is noted that (a) Proteus is only one of several species recited as exemplary of primary gram negative urinary pathogens; (b) none of the claims are limited to detection, etc. of Proteus (claim 24 recites two Proteus species as part of a Markush group, but also recites other organisms which are detected by MacConkey agar), and (c) formulations of MacConkey agar are known which do allow for growth of Proteus, specifically Proteus mirabilis. Support for this may be found on page 289 of the Difco manual, supplied by applicant. The Difco manual also teaches that MacConkey agar supports growth of Proteus but inhibits *swarming* (pages 289-290). Swarming is not the same as growth. For all of these reasons, applicant's arguments regarding MacConkey agar are not convincing.

In response to the argument that the medium can be claimed functionally, applicant should note that the MacConkey agar taught by LIBMAN has the same "function" as the uropathogenic specific medium recited in the claims; i.e. is selective for gram negative organisms which cause 85-90% of urinary tract infections. It is further noted that the Opinion in In re Swinehart (169 USPQ 226) stated that:

"Functional" terminology may render a claim quite broad. By its own literal terms a claim employing such language covers any and all embodiments which perform the recited function. Legitimate concern often properly exists, therefore, as to whether the scope of protection defined thereby is warranted by the scope of enablement indicated and provided by the description contained in the specification.

It is again noted that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). As set forth above, the MacConkey agar of LIBMAN has the same function as that set forth for the uropathogenic specific medium of the claims. It is noted that uropathogenic specific medium comprising antibiotics/inhibitors are described on page 12 as being preferred embodiments of the media for use in the inventive method, but the specification does not teach that a UTI medium must necessarily comprise antibiotics. It is also noted that the CHEN declaration states on page 5 that it is NECESSARY to incorporate antibiotics into the inventive UTI medium. It is not clear whether CHEN is referring to the UTI medium itself, or to the interpretation medium. The examiner agrees that the interpretation medium must comprise an antimicrobial agent, as this limitation is recited in the claims. However, if CHEN refers to the UTI medium itself, then applicant is advised that this may be interpreted as a teaching that antibiotics are an essential element of a UTI medium, and may result in a rejection of the claims for omitting essential elements. As no evidence is presented, and it is unclear to which medium CHEN is referring in his declaration, applicant is merely advised that this particular argument is confusing.

In response to the argument on page 6 of the CHEN declaration that adding an antimicrobial agent to the medium of the inventive method will not change the "bacterial resistance pattern" of the medium, which CHEN apparently is arguing as an unexpected result,

it is noted that no evidence is supplied showing that MacConkey agar would be expected to display a change in "bacterial resistance pattern" upon addition of antimicrobial agent.

In response to the argument that JOHNSON, LIBMAN, and the MCB do not teach a signal-generating substrate, applicant is reminded that the rejection is made over a combination of references wherein CARR teaches a signal generating substrate. In response to the argument that MacConkey agar does not produce color in the presence of Proteus, it is noted that at least one of the substrates of CARR react with Proteus mirabilis to produce a detectable color/signal (col. 7, lines 35-60). AS Proteus does grow on MacConkey agar, the medium comprising fluorogenic substrates in the method made obvious by the combination of JOHNSON, LIBMAN, and the MCB, further in view of CARR would be expected to produce a signal in the presence of Proteus.

For all of the reasons set forth above, the examiner maintains that MacConkey agar is a UTI medium, therefore the combination of JOHNSON, LIBMAN, and the MCB, further in view of CARR makes obvious the claims.

Amended claim 26 is newly rejected under 35 U.S.C. 103(a) as being unpatentable over JOHNSON (US 4,077,845) in view of LIBMAN *et al.* (US 4,046,138), the MANUAL OF CLINICAL MICROBIOLOGY (MCB), and CARR *et al.* (IDS ref: US 5,064,756) as applied to claims 1-24 above, and further in view of BROCCO.

Applicant's arguments with respect to claim 26 have been considered but are moot in view of the new ground(s) of rejection. Arguments set forth in the response of 3/26/01 are addressed below.

The claims recite a method of detecting and determining antimicrobial susceptibility of uropathogens, as set forth above.

JOHNSON LIBMAN, the MCB, and CARR make obvious a method of detecting and determining antimicrobial susceptibility of uropathogens, as set forth above

BROCCO teaches a method of determining susceptibility of uropathogens, to amoxicillin and a clavulanic acid mixture (p. 5, line 8-p. 6, line 7 and p. 9, line 4-p. 10, line 15).

It would have been obvious at the time of invention to include the amoxicillin and clavulanic acid of BROCCO as antimicrobial agents in the method of JOHNSON LIBMAN, the MCB, and CARR where the motivation would have been to test susceptibility of microorganisms, specifically urinary pathogens, to any known antibiotics, as suggested by JOHNSON, in order to determine an appropriate course of treatment for a subject infected with the microorganisms.

Applicant argues that BROCCO does not teach a selective medium and teaches use of sterile medium and a sterile device. In response, it is noted that the rejection is made over a combination of references wherein BROCCO is relied upon only for his teaching of antibiotics which may be used in methods of determining susceptibility. AS previously set forth, both JOHNSON and LIBMAN teach nonsterile samples. The argument regarding sterile medium is confusing because any medium before addition of a sample should be sterile in order to prevent growth of adventitious organisms during storage. Even a selective medium should be sterilized or freshly made from sterile ingredients immediately before use in order to prevent growth of organisms NOT present in the sample. The argument with regard to cross-reactivity is not germane as the MacConkey agar in the method of JOHNSON LIBMAN, the MCB, and CARR does not comprise an antibiotic. For these reasons, claim 26 is obvious.

Conclusion

Claims 20-24 and 26 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a Patent Analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
~~GROUP 1800~~
AU1631

Marjorie A. Moran
June 8, 2001